IV. REMARKS/ARGUMENTS

A. Status of the Claims

Claims 24, 28-32, 34, 35, 38-40, 43 and 92-94 are pending. Claims 33, 36 and 37 have been cancelled without prejudice. Claims 1-23 and 44-91 were previously withdrawn. Claim 31 has been amended. Applicants submit that no new matter has been added by virtue of these amendments.

B. Objections to the Specification

With regard to objection #5 on page 2 of the Office Action, Applicant has requested amendment of the paragraph as indicated in section II above.

With regard to objection #6 on page 2 of the Office Action, Applicants believe this language to be clear. As explained in the specification at page 18, lines 19-24, monoclonal antibodies can be generated in two ways in accordance with the present invention: i) by in-vitro immunization or ii) in-vivo immunization. Metabolic decomposition of an analog carrier conjugate can only take place if immunization is in-vivo. This is clear from the definition of metabolism provided in The Dictionary of Biology, 9th Ed., page 392 (1996) which states that metabolism is the "sum of the physical and chemical processes occurring within a living organism." Accordingly, metabolism is an in-vivo process. The rejected sentence states that if the analog-carrier conjugate would be subject to metabolic decomposition, in-vivo, then in vitro immunization is preferred. No ambiguity exists.

With regard to objection #7 on page 2 of the Office Action, support for the range of the dissociation constant can be found in claims 7, 29, 68 and 83 as originally filed.

With regard to objection #8 on page 3 of the Office Action, support for the subject matter claimed in claims 36 and 37 can be found in claims 36 and 37 as originally filed. Notwithstanding, Applicants point out that claims 36 and 37 have been cancelled.

Applicants acknowledge the Examiner's renumbering of claims 44-46 to claims 92-94.

C. 35 U.S.C. § 112, Second Paragraph

With regard to the rejection of claims 29, 39 and 40 as being indefinite, Applicants believe one skilled in the art would understand the terms "about" and "approximately" to mean to come near or close, as in degree, or quantity (The American Heritage® Dictionary of the English Language, Fourth Edition, 2000). Further, use of these terms can be seen in many Registered patents (See: e.g., U.S. Patent No. 6,649,773; 6,649,761; 6,649,660; 6,649,649; 6,649,607; 6,649,183; and 6,647,980). Accordingly, claim 29 and amended claims 39 and 40 are not indefinite. Therefore, the Examiner's rejection should be removed.

With regard to the rejection of claims 36 and 37 as being indefinite, claims 36 and 37 have been cancelled, without prejudice.

D. Rejections under 35 U.S.C. § 102

In the Office Action, the Examiner made the following rejections:

Claims 24, 28, 31, 32, 34, 36-40, 43 and 92-94 were rejected under 35 U.S.C. § 102(e) as being anticipated by Kauver, et al. (U.S. Patent No. 5,674,688). The Examiner argued, *inter alia*, that Kauver, et al. teach:

> "identifying one or more key component fragments... coupling... analogs ... to a carrier molecule to construct ... analog carrier conjugates... generat[ing] a panel of monoclonal antibodies *in vitro* and *in-vivo*... assaying the monoclonal antibodies to determine specificity... immobilizing the monoclonal antibodies on a support..., conducting a series of in-vitro assays... to screen one or more compounds of interest."

Applicants respectfully traverse this rejection. The '688 patent does not disclose numerous elements of independent claims 24, 93 and 94 and therefore cannot anticipate these claims.

It is important to note at the outset that the present invention provides a method for identifying compounds of interest which have binding affinity for a target receptor. Specifically, independent method claim 24 recites:

> **24.** A method of identifying one or more compounds of interest **which have binding affinity for a target receptor** comprising:
> (a) **identifying one or more key component fragments** of one or more chemical compounds having binding affinity for a target receptor wherein said key component fragment is a portion of a molecule which contributes to the binding affinity of that molecule for the target receptor;
> (b) coupling one or more analogs of the one or more chemical compounds to a carrier molecule to construct one or more analog-carrier conjugates, said analogs containing one or more of the key component fragments, said analogs being coupled to the carrier **such that one or more of the key component fragments are exposed**;
> (c) utilizing the analog-carrier conjugates to generate monoclonal antibodies in vivo or in vitro that are **able to define the exposed key component fragments;** and
> (d) **measuring the dissociation constant** for the binding of the monoclonal antibodies to the analogs to determine which monoclonal antibodies exhibit the **strongest binding**;
> (e) immobilizing the monoclonal antibodies having the **strongest binding** on a support; and
> (f) conducting a series of in-vitro assays utilizing said immobilized monoclonal antibodies to screen one or more compounds of interest. (emphasis added)

In contrast, the '688 patent purportedly describes methods for determining the analyte composition of a sample. The method of the '688 patent generally comprises: i) contacting an unknown sample with at least two specifically reactive reagents, e.g., antibodies, each of which is reactive to some differing degree with the members of a class of suspected analytes; ii) obtaining a profile of reactivity (survey of characteristics hereinafter "SC profile") for the sample; and iii) matching the SC profile with a predetermined SC profile of known compositions (See: col. 2,

lines 28-33). SC profiles are obtained by: i) contacting a set of analyte compositions with a panel of reagents, e.g., antibodies, reactive with the analyte compositions; and ii) plotting the SC profile (See: col. 2, lines 38-45).

Significantly, in the '688 patent, the monoclonal antibodies are reactive to differing degrees with the analytes and the analytes are identified based on a profile of reactivity. In sharp contrast, the monoclonal antibodies of the present invention exhibit the strongest binding.

Further, the '688 patent does not teach "identifying one or more key component fragments of a compound(s) having a binding affinity for a target receptor" (step a) as suggested by the Examiner. The Examiner specifically relies on claim 1 of the '688 patent for his rejection. However, claim 1 of the '688 patent recites, in pertinent part, the steps of: i) contacting a sample analyte with at least two specifically reactive agents; ii) detecting and measuring the amount of reactivity of the reagents with the sample, each measurement determining a value for a characteristic parameter for the sample; iii) compiling the values to obtain a survey of characteristics profile (SC) for the sample; iv) comparing the SC of the sample with a reference set of SC profiles from known compositions; and v) identifying the analyte composition based on the SC profiles. Nowhere does claim 1 or the specification of the '688 patent teach identifying one or more key component fragments of a compound having a binding affinity for a target receptor as recited in step a of the independent claims of the present invention.

Further, the Examiner asserts that the '688 patent (column 8, lines 25-55) teaches "coupling one or more analogs of the compounds to a carrier molecule to construct one or more analog-carrier conjugates." The Examiner does not address the claim element of independent claim 24 step b, wherein "said analogs being coupled to the carrier such that one or more of the key component fragments are exposed...." Although the '688 patent does generally disclose conjugating analogs to BSA or KLH carriers, it does not even disclose identifying key component fragments and therefore could not possibly disclose coupling analogs to a carrier such

that the key component fragments are exposed.

Similarly, the Examiner correctly asserts that the '688 patent teaches utilizing an analog carrier conjugate to generate a panel of monoclonal antibodies, but the Examiner leaves out the portion of independent claim 24, step c, which states that the monoclonal antibodies "are able to define the exposed key component fragments." Nowhere is this concept taught in the '688 patent.

Next, the Examiner improperly paraphrases step d of independent claim 24 to read, "assaying the monoclonal antibodies to determine specificity." However, claim 24, step d, actually requires "measuring the dissociation for the binding of the monoclonal antibodies to the analogs to determine which monoclonal antibodies exhibit the strongest binding". Determining specificity is not the same thing as determining strongest binding. Further, in the '688 patent, the specificity is different for each monoclonal antibody, with the differences used as a means of identifying the analyte(s) in question. There is no teaching of strong binding. In contrast, finding monoclonal antibodies having the strongest binding is a critical element of the present claim 24. Moreover, the Examiner's support for the specificity (Claim 11 of the '688 patent) is inaccurate. Claim 11 of the '688 patent is directed to preparation of a reference set of specificity characteristics (SC profiles). It does not teach determining the monoclonal antibodies exhibiting the strongest binding for the key component fragments. Not surprisingly, there also is no teaching in the '688 patent of "measuring the dissociation constant" (claim 24, step d).

In the Office Action, the Examiner also generically says that the '688 patent teaches "immobilizing the monoclonal antibodies on a support. However, claim 24, step e specifically calls for "immobilizing the antibodies having the strongest binding on a support". The '688 patent does not teach determining the antibodies having the strongest binding, and therefore, cannot possibly teach immobilizing the antibodies having the strongest binding on a support.

To anticipate a claim, a single source must contain all of the elements of the claim. See: *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1379, 231 U.S.P.Q. 81, 90 (Fed. Cir. 1986), *Atlas Powder Co. v. E.I. du Pont De Nemours & Co.*, 750 F.2d 1569, 1574, 224 U.S.P.Q. 409, 411 (Fed. Cir. 1984); *In re Marshall*, 578 F.2d 301, 304, 198 U.S.P.Q. 344, 346 (C.C.P.A. 1978). As seen from the discussion above, many elements of present claim 24 are missing from the '688 patent. As the '688 patent does not teach each and every claim element of independent claim 24, it cannot be anticipated by the '688 patent. As such, claims 28-32 and 34-43 which depend from claim 24 are also not anticipated by the '688 patent. Therefore, the Examiner's rejection should be removed.

Claims 93 and 94 of the present invention reads as follows:

93. A method of identifying one or more compounds of interest which have **binding affinity for a target receptor** comprising:

(a) **identifying one or more key component fragments** of one or more chemical compounds having binding affinity for a target receptor wherein said key component fragment is a portion of a molecule which contributes to the binding affinity of that molecule for the target receptor;

(b) coupling one or more analogs of the one or more chemical compounds to a carrier molecule to construct one or more analog-carrier conjugates, said analogs containing one or more of the key component fragments, said analogs being coupled to the carrier **such that one or more of the key component fragments are exposed**;

(c) utilizing two or more analog-carrier conjugates to generate a panel of monoclonal antibodies, wherein each analog carrier conjugate **defines a key component fragment** of the one or more chemical compounds, and wherein the analog-carrier conjugates together define the entire surface conformation of the one or more chemical compounds;

(d) assaying the monoclonal antibodies to determine which are **most specific** for the key component fragments of the one or more chemical compounds and which bind to the one or more chemical compounds;

(e) immobilizing the monoclonal antibodies which are **most specific** for the key component fragments on a support; and

(f) conducting a series of in-vitro assays utilizing said immobilized

monoclonal antibodies to screen one or more compounds of interest. (emphasis added)

94. A method of identifying one or more compounds from synthetic products which have **binding affinity for a target receptor** comprising:

(a) **identifying one or more key component fragments** of one or more chemical compounds having binding affinity for a target receptor wherein said key component fragment is a portion of a molecule which contributes to the binding affinity of that molecule for the target receptor;

(b) coupling one or more analogs of the one or more chemical compounds to a carrier molecule to construct one or more analog-carrier conjugates, said analogs containing one or more of the key component fragments, said analogs being coupled to the carrier **such that one or more of the key component fragments are exposed**;

(c) utilizing two or more analog-carrier conjugates to generate a panel of monoclonal antibodies, and wherein each analog carrier conjugate **defines a key component fragment** of the one or more chemical compounds, and wherein the analog-carrier conjugates together define a portion of the entire surface conformation of the one or more chemical compounds;

(d) assaying the monoclonal antibodies to determine which are **most specific** for the key component fragments of the one or more chemical compounds and which bind to the one or more chemical compounds;

(e) immobilizing the monoclonal antibodies which are **most specific** for the key component fragments on a support; and

(f) conducting a series of in-vitro assays utilizing said immobilized monoclonal antibodies to screen one or more compounds from synthetic products. (emphasis added)

As with claim 24 above, a number of elements set forth in claims 93 and 94 cannot be found in the '688 patent. Therefore, the '688 patent cannot anticipate claims 93 and 94. Elements of claims 93 and 94 not found in the '688 patent are discussed below.

It is worth repeating that the '688 patent discloses monoclonal antibodies which are reactive to differing degrees with the analytes and that the analytes are identified based on a profile of reactivity. In sharp contrast, the monoclonal antibodies of present claims 93 and 94 are assayed to determine which are <u>most specific</u> for the key component fragments.

Further, the '688 patent does not teach "identifying one or more key component fragments of a compound(s) having a binding affinity for a target receptor" (step a of claims 93 and 94) as suggested by the Examiner. The Examiner specifically relies on claim 1 of the '688 patent for his rejection. However, claim 1 of the '688 patent recites, in pertinent part, the steps of: i) contacting a sample analyte with at least two specifically reactive agents; ii) detecting and measuring the amount of reactivity of the reagents with the sample, each measurement determining a value for a characteristic parameter for the sample; iii) compiling the values to obtain a survey of characteristics profile (SC) for the sample; iv) comparing the SC of the sample with a reference set of SC profiles from known compositions; and v) identifying the analyte composition based on the SC profiles. Nowhere does claim 1 or the specification of the '688 patent teach identifying one or more key component fragments of a compound having a binding affinity for a target receptor as recited in step a of independent claims 93 and 94 of the present invention.

Further, the Examiner asserts that the '688 patent (column 8, lines 25-55) teaches "coupling one or more analogs of the compounds to a carrier molecule to construct one or more analog-carrier conjugates." The Examiner notably fails to address the claim element of independent claims 93 and 94, step b, wherein "said analogs being coupled to the carrier such that one or more of the key component fragments are exposed...." Although the '688 patent does disclose conjugating analogs to BSA or KLH carriers, it does not disclose identifying key component fragments, and therefore could not possibly disclose coupling analogs to a carrier such that the key component fragments are exposed.

Similarly, the Examiner correctly asserts that the '688 patent teaches utilizing an analog carrier conjugate to generate a panel of monoclonal antibodies, but the Examiner leaves out the portion of independent claims 93 and 94, step c, which states that each analog carrier conjugate defines a key component fragment. Nowhere is this concept taught in the '688 patent.

Next, the Examiner improperly paraphrases claim step d) of independent claims 93 and 94 to read, "assaying the monoclonal antibodies to determine specificity." However, step d of claims 93 and 94 actually require assaying the monoclonal antibodies to determine which are "most specific for the key component fragments". Determining specificity is not the same thing as determining most specific binding. Further, in the '688 patent, the specificity is different for each monoclonal antibody, with the differences used as a means of identifying the analyte(s) in question. There is no teaching of most specific binding. In contrast, finding monoclonal antibodies having the most specific binding is a critical element of the present claims 93 and 94. Moreover, the Examiner's support for the specificity (Claim 11 of the '688 patent) is inaccurate. Claim 11 of the '688 patent is directed to preparation of a reference set of specificity characteristics (SC profiles). It does not teach determining the monoclonal antibodies most specific for the key component fragments.

In the Office Action, the Examiner also generically says that the '688 patent teaches "immobilizing the monoclonal antibodies on a support. However, step e of independent claims 93 and 94 specifically call for "immobilizing the antibodies which are most specific for the key component fragments on a support." The '688 patent does not teach immobilizing the most specific antibodies on a support.

As the '688 patent does not teach each and every claim element of independent claims 93 and 94, they cannot be anticipated by the '688 patent.

Claims 24, 28, 30, 32, 35-40, 43 and 92 were rejected under 35 U.S.C. § 102(e) as being anticipated by Buechler, *et al.* (U.S. Patent No. 5,939,272). The Examiner argued, *inter alia*, that Buechler, *et al.* specifically teaches "identifying one or more key component fragments..., measuring the dissociation constant..., immobilizing the monoclonal antibodies having the strongest binding on a support." The Examiner also argued that Buechler, *et al.* "suggests that these in-vitro assays utilizing said immobilized monoclonal antibodies could be used to screen

one or more compounds of interest."

In rendering this rejection, the Examiner has taken broad concepts from various parts of the specification of the '272 patent. What he has failed to do, however, is show that the '272 patent contains all of the elements set forth in the present invention.

The '272 patent purportedly describes ligand-receptor assays for the detection of selected analytes and their concentrations in a fluid sample. The ligand receptor assays described in the '272 patent rely on the binding of the ligands by receptors, e.g., antibodies, to determine the concentration of the ligands in the sample (See: '272 patent col. 1, line 65 through col. 2, line 21). The claims of the present invention, however, are not directed to the detection of analytes and their concentrations from a sample by binding ligands to a receptor. The claims of the present invention provide a method for identifying compounds of interest which have binding affinity for a target receptor, not by binding the compounds of interest to the receptor itself.

The Examiner's cherry picking of concepts can be seen in his assertion that the '272 patent teaches identifying one or more key component fragments. In the Office Action, the Examiner implies that the key component fragments of the present invention are the same element as the Fc fragment of mouse IgG as described in the '272 patent. This is not an accurate characterization of the '272 patent. What the '272 patent is actually referring to is the optional use of goat-anti-mouse Fc, an affinity-purified goat IgG antibody against the Fc fragment of mouse IgG, to provide a means for removing ligand receptors from the reaction mixture. According to the '272 patent, the goat-anti-mouse Fc may be included whenever it is necessary or desirable to prevent ligand analogue conjugate:ligand receptor complexes in the reaction mixture from contacting the terminal solid phase, generally in a situation when an enormous surplus of analyte might saturate antibodies. The consequence of this is a low bonding affinity of signal antibody to solid phase and is known as a "hook effect". Indeed, the '272 patent at col. 16, lines 44-66, specifically states:

> Such an optional means is necessary if, for example, ligand analogue conjugate:ligand receptor complex in the reaction mixture dissociates to a significant extent during incubation with the terminal solid phase such that terminal solid phase immobilized ligand receptor could bind dissociated ligand analogue conjugate and result in a detectable signal even in the absence of target ligand. The optional means for removing ligand receptors from the reaction mixture may be any device means for binding ligand receptors so that they are removed from the reaction mixture prior to contacting the reaction mixture with the terminal solid phase. For example, such an optional means may consist of (ligand receptor) receptors and solid phase supports for immobilization of these (ligand receptor) receptors, such that through binding of reaction mixture ligand receptors to (ligand receptor) receptors immobilized on the solid phase support of the optional means, the ligand receptors and ligand receptor associated complexes are prevented from contacting ligand receptors bound to the terminal solid phase. Examples of receptors and solid phases which may be useful in constructing optional means for the removal of ligand receptors include anti-antibody antibodies such as goat-anti-mouse IgG or goat-anti-mouse Fc...

Again, the goat anti mouse Fc fragment is merely chosen as a means of removing excess ligand receptors in the reaction mixture (mouse monoclonal antibodies against a ligand whose concentration is to be determined) by using an antibody that recognizes the mouse-specific portion of the antibody.

In contrast, the key component fragments of the present invention are defined in independent claims 24, 93 and 94 as being "a portion of a molecule which contributes to the binding affinity of that molecule for the target receptor". Further, the key component fragments claimed in the present invention are not used to remove excess ligand receptors. They are coupled to a carrier molecule to construct one or more analog-carrier conjugates, such that one or more of the key component fragments are exposed. The analog-carrier conjugates are then utilized to generate monoclonal antibodies in vivo or in vitro that are able to define the exposed key component fragments. None of these steps are taught in the '272 patent.

The Examiner also is incorrect in stating that the '272 patent teaches the step of measuring of dissociation constant found in claim 24 of the present invention. However, the mere fact that dissociation constant is measured in the '272 patent does not by necessity result in the measurement of the monoclonal antibodies exhibiting the strongest binding. Indeed the '272 patent does not teach step (d) of claim 24 wherein the dissociation constant is measured for the binding of the monoclonal antibodies to the analogs to determine which monoclonal antibodies exhibit the **strongest binding.** The '272 patent also does not teach claim 24 step e, wherein the monoclonal antibodies having the **strongest binding** are immobilized on a support.

The '272 patent also does not teach steps d and e of claims 93 and 94 which call for assaying the monoclonal antibodies to determine which are **most specific** for the key component fragments of the one or more chemical compounds and which bind to the one or more chemical compounds and then immobilizing the monoclonal antibodies which are **most specific** for the key component fragments on a support.

Accordingly, the '272 patent does not include a number of the elements contained in claims 24, 93 and 94 of the present invention. Therefore the '272 patent cannot anticipate these claims. As claims 28-32 and 34-43 depend from claim 24, these claims are also not anticipated by the '272 patent.

E. Rejection under 35 U.S.C. § 103

Claim 29 was rejected under 35 U.S.C. § 103(a) as being obvious over Kauver, et al. The Examiner admitted that the method of Kauver et al. "fails to recite the specific feature of generating monoclonal antibodies with a dissociation constant in the range of 0.01 nM to 10nM. The Examiner nevertheless argued that it would have been obvious for a person of ordinary skill in the art to generate monoclonal antibodies with dissociation constants within this particular range...."

In response, Applicants first point out that Claim 29 depends from Claim 24. The '688 patent does not teach or suggest many of the elements of claim 24, including the elements of measuring the dissociation constant for the binding of the monoclonal antibodies to the analogs to determine which monoclonal antibodies exhibit the strongest binding and immobilizing the monoclonal antibodies having the strongest binding on a support.

It must be restated that the '688 patent purportedly describes methods for determining the analyte composition of a sample. The method of the '688 patent generally comprises: i) contacting an unknown sample with at least two specifically reactive reagents, e.g., antibodies, each of which is reactive to some differing degree with the members of a class of suspected analytes; ii) obtaining a profile of reactivity (survey of characteristics hereinafter "SC profile") for the sample; and iii) matching the SC profile with a predetermined SC profile of known compositions (See: col. 2, lines 28-33). SC profiles are obtained by: i) contacting a set of analyte compositions with a panel of reagents, e.g., antibodies, reactive with the analyte compositions; and ii) plotting the SC profile (See: col. 2, lines 38-45).

The '688 patent clearly does not teach or suggest measuring dissociation constant to determine which monoclonal antibodies exhibit the strongest binding, because differing degrees of binding are actually desirable in the '688 patent. When combined with all of the additional elements of claim 24 enumerated above in the anticipation discussion which are not taught or disclosed by the '688 patent, it becomes more than clear that the '688 patent could not possibly render the invention of claim 29 obvious.

Further, the '688 patent is directed to a very different invention. The '688 patent is directed to methods for determining the analyte composition of a sample (e.g. determining whether a urine sample contains THC or steroids), whereas claim 24 (and therefore, dependent claim 29) of the present invention provides a method for identifying compounds of interest which have binding affinity for a target receptor (e.g. searching for new chemical compounds to treat a

disease state). There is no suggestion in the '688 patent to modify the disclosed process of the '688 patent to include the missing elements identified above. Therefore, claim 29 is not obvious over the '688 patent.

In the Office Action, the Examiner also rejected Claim 30 under 35 U.S.C. § 103(a) as being obvious over Kauver, et al. in view of Harlow. The Examiner specifically argued that "methods of generating monoclonal antibodies *in-vivo* [and] *in-vitro* would be well known to a person of ordinary skill in the art...."

As with Claim 29, claim 30 is dependent from and therefore incorporates all of the limitations of claim 24. Therefore, claim 30 also is not obvious over the '688 patent.

The Harlow reference is directed to a discussion about various carrier proteins that may be utilized for coupling to a hapten to produce an immune response. In particular, the Harlow reference discusses various Kehole Limpet Hemocyanin (KLH) carrier proteins. The Harlow reference does not disclose or suggest most of the elements of present claim 24, including the identifying of key component fragments, coupling analogs to a carrier such that the key components are exposed, generating monoclonal antibodies that are able to define the exposed key component fragments, measuring the dissociation constant to determine which monoclonal antibodies exhibit the strongest binding or immobilizing the monoclonal antibodies having the strongest binding on a support. As the Harlow reference does not cure the deficiencies in the '688 patent, the combination of the '688 patent in view of the Harlow reference cannot render present claim 30 obvious.

Claim 29 also was rejected under 35 U.S.C. § 103(a) as being obvious in view of Buechler, et al. The Examiner argued that the method of Buechler, *et al.* "fails to recite the specific feature of... a dissociation constant in the range of 0.01 nM to 10nM. The Examiner again specifically argues that it would have been obvious for a person of ordinary skill in the art

to generate monoclonal antibodies with dissociation constants within this particular range...."

As explained above, claim 29 depends from and therefore incorporates the limitations of claim 24. As also explained above, the Buechler patent is directed to ligand-receptor assays for the detection of selected analytes and their concentrations in a fluid sample. The ligand receptor assays described in the '272 patent rely on the binding of the ligands by receptors, e.g., antibodies, to determine the concentration of the ligands in the sample (See: '272 patent col. 1, line 65 through col. 2, line 21). This bears no relation to claim 24 (and therefore, dependent claim 29) of the present invention which provides a method for identifying compounds of interest which have binding affinity for a target receptor by:

> (a) identifying one or more key component fragments of one or more chemical compounds having binding affinity for a target receptor wherein said key component fragment is a portion of a molecule which contributes to the binding affinity of that molecule for the target receptor;
>
> (b) coupling one or more analogs of the one or more chemical compounds to a carrier molecule to construct one or more analog-carrier conjugates, said analogs containing one or more of the key component fragments, said analogs being coupled to the carrier such that one or more of the key component fragments are exposed;
>
> (c) utilizing the analog-carrier conjugates to generate monoclonal antibodies in vivo or in vitro that are able to define the exposed key component fragments; and
>
> (d) measuring the dissociation constant for the binding of the monoclonal antibodies to the analogs to determine which monoclonal antibodies exhibit the strongest binding;
>
> (e) immobilizing the monoclonal antibodies having the strongest binding on a support; and
>
> (f) conducting a series of in-vitro assays utilizing said immobilized monoclonal antibodies to screen one or more compounds of interest.

In particular, the '272 method fails to disclose or suggest many of the claimed elements of claim 24. For example, the '272 patent does not disclose or suggest coupling key component fragments of a compound to a carrier molecule to construct one or more analog-carrier

conjugates, such that one or more of the key component fragments are exposed. Nor does it disclose or suggest utilizing the analog-carrier conjugates generate monoclonal antibodies in vivo or in vitro that are able to define the exposed key component fragments. Nor does the '272 patent teach or suggest measuring the dissociation constant for the binding of the monoclonal antibodies to the analogs to determine which monoclonal antibodies exhibit the strongest binding nor of the immobilizing of the monoclonal antibodies having the strongest binding on a support.

There is no suggestion in the '272 patent to modify the disclosed process in the '272 patent to include the missing elements identified above. Clearly, the '272 patent could not possibly render the invention of claim 29 obvious.

Claim 35 was rejected under 35 U.S.C. § 103(a) as being obvious in view of Kauver, et al. in view of Buechler, et al. The Examiner admitted that the '688 patent fails to disclose chemical compounds exhibiting PDEIV inhibitor or opiate activity, but argues that the '272 patent suggests a compound exhibiting opiate activity (opiates) for the purpose of creating a drug abuse panel. Therefore, the Examiner argued that "... it would have been obvious for a person of ordinary skill in the art to use the method of Kauver to test for chemical compounds [sic] that exhibit opiate activity."

As with Claim 29, claim 35 is dependent from and therefore incorporates all of the limitations of claim 24. For the reasons cited above for claims 29 and 30, claim 35 also cannot be rendered obvious in view of '688 patent.

The Examiner cited the '272 patent for its alleged teachings of use of a compound exhibiting opiate activity to create a drug abuse panel. The Examiner fails to point out that the '272 patent does not teach or suggest PDEIV activity. Further, the use of a compound exhibiting opiate activity to create a drug abuse panel has no relation to the identifying of a compound having PDEIV activity using the steps of claim 24 of the present invention. Finally, as discussed

above, the '272 patent is missing a number of claim elements set forth in independent claim 24. As the '272 patent is missing many of the same elements of present claim 24 that are missing from the '688 patent, the '272 patent cannot possibly cure the deficiencies in the '688 patent. As a result, present claim 35 is obvious over the combination of the '688 patent in view of the '272 patent.

In addition, Claim 31 was rejected under 35 U.S.C. § 103(a) as being obvious over Buechler, et al. in view of Keiser. The Examiner again argued that "methods of generating monoclonal antibodies *in-vivo* [and] *in-vitro* would be well known to a person of ordinary skill in the art...."

As with Claim 29, claim 31 is dependent from and therefore incorporates all of the limitations of claim 24. For the reasons cited above for claim 29, claim 31 also cannot be rendered obvious in view of the '272 patent .

The Keiser reference is directed to the production and partial characterization of a series of monoclonal antibodies directed against the PG monomer-HA binding region and the link proteins of bovine nasal cartilage. The Keiser reference does not disclose or suggest most of the elements of present claim 24, including the identifying of key component fragments, coupling analogs to a carrier such that the key components are exposed, generating monoclonal antibodies that are able to define the exposed key component fragments, measuring the dissociation constant to determine which monoclonal antibodies exhibit the strongest binding or immobilizing the monoclonal antibodies having the strongest binding on a support. As the Keiser reference does not cure the deficiencies in the '272 patent, the combination of the '272 patent in view of the Keiser reference cannot render present claim 30 obvious.

Finally, Claim 34 was rejected was under 35 U.S.C. § 103(a) as being obvious over Buechler, et al. in view of Harlow, et al. and Kauver, et al. The Examiner argued that "... it would be obvious to a person of ordinary skill in the art to use KLH as a carrier molecule."

As with Claims 29 and 30, claim 35 is dependent from and therefore incorporates all of the limitations of claim 24. For the reasons cited above for claims 29 and 30, claim 35 also cannot be rendered obvious in view of the '272 patent.

As discussed above, the Harlow patent is directed to a discussion about various carrier proteins that may be utilized for coupling to a hapten to produce an immune response. In particular, the Harlow reference discusses various Kehole Limpet Hemocyanin (KLH) carrier proteins. It fails to teach many of the steps of claim 24 of the present invention including failing to teach or suggest the steps of claim 24 of assaying the monoclonal antibodies to determine which are most specific for the key component fragments of the one or more chemical compounds and which bind to the one or more chemical compounds and then immobilizing the monoclonal antibodies which are most specific for the key component fragments on a support. Likewise, the '688 patent also fails to teach many of the same steps of claim 24 of the present invention, including assaying the monoclonal antibodies to determine which are most specific for the key component fragments of the one or more chemical compounds and which bind to the one or more chemical compounds and then immobilizing the monoclonal antibodies which are most specific for the key component fragments on a support. Therefore, for at least this reason, these references cannot cure the deficiencies in the '272 patent.

CONCLUSION

In view of this response, Applicants submit that the present application is now in condition for allowance. An early and favorable action on the merits is earnestly solicited.

Respectfully submitted,

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